

REMARKS

In the Official Action dated November 28, 2005, claims 18-20 are pending and under examination. Claims 18-20 are rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1-21 of U.S. Patent No. 6,083,512 in view of Farmers and Consumers Market Bulletin (Department of Agriculture, Atlanta, Georgia, 70(24): 1984, page 1, 12, ill.). Claims 18 and 20 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Seifert (*Deutsche Tierarzliche Wochem.* 90(7): 274-279, 1983) in view of Geresi et al. (*Ann. Immunol. Hung.* 25: 37-40, 1985), Farmers and Consumers Market Bulletin, and Kensil (U.S. Patent No. 5,057,540). Claim 19 is rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Seifert, Geresi et al., Farmers and Consumers Market Bulletin, and Kensil as applied to claims 18 and 20 above, and further in view of Green et al. (*The Veterinary Record* 120: 435-439, 1987). The application is also objected to for allegedly failing to comply with the requirements of 37 C.F.R. §§1.821-1.825.

This Response addresses each of the Examiner's rejections and objections. Specifically, Applicants have canceled claim 18, and have amended claim 19 to depend from claim 20. It is believed that in view of the amendments to the claims and the following remarks, the present application is in condition for allowance. Favorable consideration of all pending claims is therefore respectfully requested.

Regarding the Examiner's objection to the application based on 37 C.F.R. §§1.821-1.825, the Examiner has not set forth the specific reasons for raising this objection. Applicants have reviewed the entire application and have not identified sequences anywhere

in the application. Withdrawal of the objection to the application is therefore respectfully requested.

With respect to the obviousness-type double patenting rejection of Claims 18-20 based on U.S. Patent No. 6,083,512 in view of Farmers and Consumers Market Bulletin, Applicants acknowledge that the rejection can be overcome by timely filing a terminal disclaimer, to disclaim the term of the issuing patent in excess of the term of the '512 patent. Applicants intend to file a terminal disclaimer once the Examiner determines that the claims, as presently recited, are otherwise allowable.

With respect to the §103(a) rejection of claims 18 and 20 based on Seifert in view of Geresi et al., Farmers and Consumers Market Bulletin, and Kensil, the Examiner alleges that Seifert teaches the use of a saponin adjuvant in the formulation of a multivalent clostridial vaccine. According to the Examiner, Seifert teaches the production of a toxoid vaccine from three apparently different strains of Clostridial pathogens. The toxoid was mixed with anthrax spores in saponin and was administered to animals. The Examiner alleges that the vaccine taught by Seifert provided a marked protective effect (see page 2). The Examiner contends that the Seifert reference differs from the claimed invention by not including antigens from a respiratory virus or multiple *Clostridium* serotypes/species.

However, the Examiner contends that Geresi teaches the formulation of multivalent clostridial vaccine compositions, which also contain a viral antigen. The Examiner further states that Farmers and Consumers Market Bulletin also discloses a clostridial vaccine composition that includes a viral immunogen. Additionally, the Examiner alleges that Kensil shows that the adjuvant activity of saponin is effective for viruses.

Therefore, the Examiner concludes that it would have been *prima facie* obvious to one having ordinary skill in the art, at the time that the invention was made, to modify the Seifert vaccine by adding any desired additional clostridial components as taught by Geresi or Farmers and Consumers Market Bulletin, and include a respiratory viral antigen as taught by Farmers and Consumers Market Bulletin. The Examiner is of the opinion that as evidenced by Geresi and Farmers and Consumers Market Bulletin, it is conventional to combine the multivalent clostridial vaccine with viral components; and as evidenced by both Seifert and Kensil, saponin is an effective adjuvant for either a clostridial or viral antigen.

In response, Applicants respectfully submit that the rejection of claim 18 is rendered moot in view of the cancellation of claim 18. Applicants further submit that contrary to the Examiner's contentions, Seifert does not provide sufficient teaching to render obvious the vaccine composition as presently recited.

In the first instance, although Seifert claims that the vaccine composition disclosed therein provided a marked protective effect against anaerobic infections, the reference does not present any actual data of vaccination and simply refers to a dissertation by Corssmeier-Ressmann (1983) for a detailed report of the results of certain field experiments. See page 2, middle paragraph and page 22, first paragraph of the English translation of Seifert. Applicants draw the Examiner's attention to the fact that positive results of field trials do not necessarily represent that vaccinated animals were protected against challenges by virulent *Clostridium*. In fact, the limitations of the field studies are stated in the Seifert reference itself. See, page 6, second paragraph, and page 12, first paragraph of the English translation of Seifert, where it is indicated that the deaths observed in field studies could also be caused by anthrax, instead of *Clostridium* pathogens. Therefore, the Seifert reference does not

provide a clear showing that the alleged protective effects observed in vaccinated animals resulted from protection against virulent *Clostridium* pathogens, rather than protection against pathogens such as anthrax or *P. multocida*, which are also present in the vaccine composition disclosed therein.

Furthermore, Applicants respectfully submit that the Seifert reference does not clearly teach that the use of saponin alone as the adjuvant would be effective for clostridial antigens. In Seifert, the clostridial immunogens were mixed with "10 million *B. anthracis*/STERNE spores in saponin" prior to administration to calves. See, page 2, middle paragraph, lines 1-2 of the English translation of Seifert. Applicants respectfully submit that the *B. anthracis*/STERNE spores included in the composition of Seifert are believed to also provide adjuvant activity. In support of Applicants' position, Applicants provide herewith an article by Delpy et al. (*Compt. Rend.* 228: 1768-1769, 1949), together with an English translation thereof (**Exhibit 1**). The article indicates the use of anthrax spores both as antigen and as adjuvant (see page 2, Item 2 of the English translation of the article). Therefore, Applicants respectfully submit that Seifert does not teach or remotely suggest that when a saponin adjuvant is the sole adjuvant component in a multicomponent clostridial vaccine, the vaccine would have any protective efficacy.

As described in the present application, there was no recognition in the art that a water-soluble adjuvant such as saponin could be used as a sole adjuvant to enhance the immunogenicity of a multicomponent clostridial vaccine. Prior to the present invention, it was generally recognized that clostridial toxoids were soluble proteins of relatively low antigenicity and poor stability; and thus, clostridial vaccines required adjuvants, typically, aluminum compounds, in order to increase antigenic potency and to enhance stability. The

present application demonstrates for the first time that a vaccine containing immunogens from two or more *Clostridium* species or serotypes conferred effective protection to vaccinated animals. See, e.g., the results of potency tests described at page 11 and 15, and Tables 2 and 7 of the specification.

Applicants further respectfully submit that the deficiencies of the Seifert reference are not cured by any of the secondary references. The cited references, either alone or in combination, do not teach or suggest a multicomponent clostridial vaccine composition formulated with saponin as the sole adjuvant, as presently claimed.

Accordingly, the obviousness rejection based on Seifert in combination with Geresi et al., Farmers and Consumers Market Bulletin, and Kensil, is overcome. Withdrawal of the rejection is therefore respectfully requested.

Claim 19 is rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Seifert, Geresi et al., Farmers and Consumers Market Bulletin, and Kensil, as applied to claims 18 and 20 above, and further in view of Green et al. Green et al. allegedly teach vaccines comprising at least 7 different serotypes/species of *Clostridium*.

As submitted above, the Seifert reference does not provide adequate teaching for an effective vaccine that protects vaccinated animals from virulent *Clostridium* pathogens. Furthermore, the Seifert reference does not clearly teach that the use of saponin alone as the adjuvant would be effective for clostridial antigens. Applicants further respectfully submit that the cited secondary references, including Green et al., do not cure the deficiencies of the Seifert reference. Therefore, the cited references, either alone or in combination, do not teach or suggest a multicomponent clostridial vaccine composition formulated with saponin as the sole adjuvant, as presently claimed.

Accordingly, the obviousness rejection of claim 19 based on Seifert in combination with Geresi et al., Farmers and Consumers Market Bulletin, Kensil, and Green et al., is overcome. Withdrawal of the rejection is therefore respectfully requested.

In view of the foregoing, it is respectfully submitted that the application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'Peter I. Bernstein', with a long horizontal flourish extending to the right.

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Enc. Exhibit 1